Movement Disorders
CLINICAL PRACTICE

CASE REPORT

Neuroleptic-like Malignant Syndrome After Battery Depletion in a Patient with Deep Brain Stimulation for Secondary Parkinsonism

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Neuroleptic malignant syndrome (NMS) is characterized by impairment of consciousness, high fever, rhabdomyolysis, rigidity, and autonomic dysfunction.[1] Although this syndrome was originally described in patients who were taking neuroleptic drugs, it may also occur in patients with Parkinson's disease (PD) during withdrawal of dopaminergic drugs and is called neuroleptic-like malignant syndrome or parkinsonism-hyperpyrexia syndrome (PHS).[1]

Case Report

We report on a 48-year-old man who had suffered since adolescence from a complex movement disorder caused by infantile hypoxic brain damage. Besides a hypokinetic-rigid syndrome with resting tremor of arms and head, he developed segmental dystonia with torticollis and orofacial dyskinesia at age 29 years. Medical treatment with levodopa (L-dopa) was started at the age of 36 years. In view of progressive symptoms of secondary parkinsonism, despite an L-dopa equivalent dose of 1100 mg, deep brain stimulation (DBS) of the subthalamic nucleus (STN) was performed when he was 40. Preoperatively, his Burke-Fahn-Marsden (BFM) motor score was 52, and his Unified Parkinson Disease Rating Scale (UPRDS) motor score off medication was 38. Cerebral magnetic resonance imaging studies demonstrated bilateral T2-weighted hyperintensities in the internal globus pallidus, possibly caused by infantile hypoxic brain damage. There was no family history of movement disorders. Quadripolar DBS electrodes (model 3389; Medtronic, Minneapolis, MN) were implanted into the STN bilaterally aided by stereotactic computed tomography and microelectrode recording. Postoperative imaging confirmed correct electrode placement. After connection of the impulse generator (Kinetra; Medtronic), the patient exhibited considerable reduction of dystonia, tremor, and hypokinetic-rigid symptoms (with stimulation on: BFM, 10.5; UPRDS motor score, 9; with stimulation off: BFM, 64; UPRDS motor score, 30). Monopolar stimulation was programmed bilaterally (pulse width, 60 μsec; frequency, 130 Hz; amplitude, 3.0 V). The dopaminergic medication could be reduced to a minimal dose of 200 mg L-dopa daily. During the following years, the patient showed further symptom increase, requiring several adaptions of stimulation parameters (monopolar/bipolar mode, different frequencies/amplitudes, symmetric/asymmetric stimulation parameters, different active contacts), and again his dopaminergic medication was increased. An unremarkable battery replacement was performed 4 years after DBS implantation. The last stimulation settings were: monopolar contacts 3 and 6, asymmetric pulse width (90 μsec; 120 μsec), frequency 130 Hz, and amplitude 2.5 V bilaterally.

Eight years after DBS implantation, the patient was admitted as an emergency case to our hospital with acute exacerbation of his movement disorder due to battery depletion, including severe resting tremor, rigidity, and dyskinesias of the upper part of his body. Despite immediate treatment with dopaminergic drugs, the patient was immobile, agitated and paranoid, tachycardic, and became incontinent of urine. His temperature rose up to 42.5°C despite symptomatic treatment. Laboratory results revealed severe rhabdomyolysis and renal failure (see Fig. 1). The occurrence of bilateral aspiration pneumonia required mechanical ventilation and tracheostomy. After stabilization, battery replacement was performed with stimulation parameters

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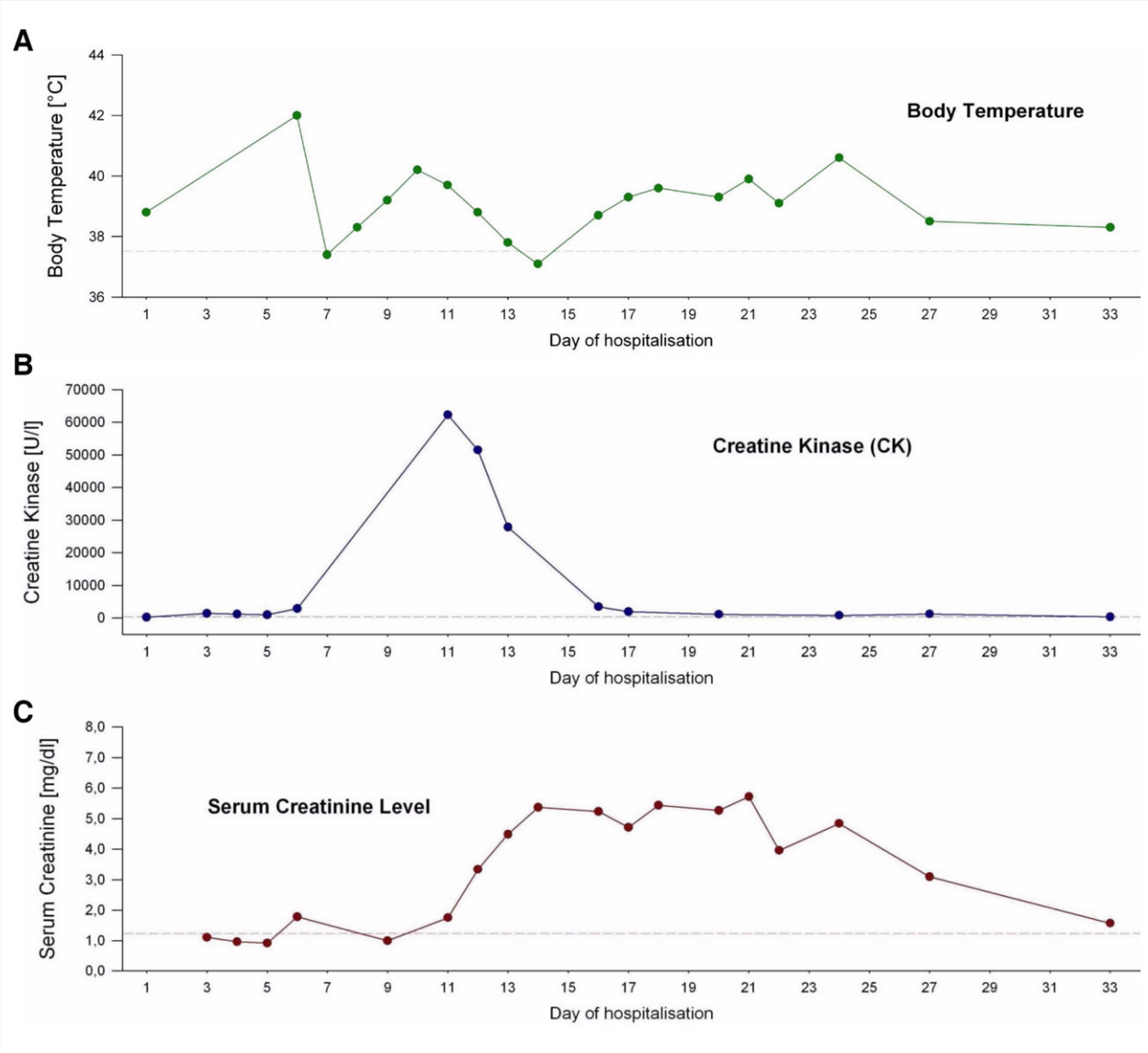

Figure 1 Time course of (A) body temperature, (B) creatine kinase, and (C) creatinine levels in a 48-year-old patient with subthalamic nucleus deep brain stimulation and parkinsonism-hyperpyrexia syndrome caused by battery depletion.

unchanged compared with previous settings. Subsequently, rigidity, tremor, and dyskinesias improved; but the patient developed thrombopenia, intermittent atrial fibrillation, and severe critical illness polyneuropathy, necessitating prolonged hospitalization. Medication comprised L-dopa 500 mg daily and piribedil 150 mg daily. Three years later, he was living in a special-care home and was able to walk with a walking frame. His overall condition was still worse than earlier with chronic STN-DBS.

Discussion

To our knowledge, this is the first report of PHS-like syndrome in a patient with *secondary* parkinsonism after battery depletion in a patient receiving chronic STN-DBS. It exemplifies PHS-like syndrome as a life-threatening medical emergency after acute DBS withdrawal. Only a few cases relating PHS to DBS in idiopathic PD have been reported.[2–5] Overall, the sudden decrease of dopaminergic transmission as a result of either abrupt preoperative drug reduction or cessation of DBS was assumed to be causative of PHS-like symptoms. PHS has been attributed to an abrupt reduction in striatal dopaminergic drive in patients without DBS.[6] In addition, distinct worsening of PD symptoms after DBS cessation has been observed as rebound phenomenon,[7] which might be an additional factor promoting PHS.

Use of the term "malignant DBS-withdrawal syndrome" (DBSWS) has been suggested when PHS-like symptoms caused by battery depletion occur.[8] The issue of DBSWS caused by a change of treatment from DBS to oral dopaminergic medication

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was subsequently addressed in a study with 15 patients who required the removal of DBS; in that study, 3 patients with advanced-stage PD who had received DBS for more than 8 years had an unfavorable course.[9]

It is notable that DBSWS is not restricted to patients with idiopathic PD and that it might also occur in younger patients. Our patient had several potential risk factors: chronic DBS (>8 years), long disease duration (over decades), and marked reduction of dopaminergic medication under chronic DBS (by 80%). The previous disease course was characterized by continuous disease progression, necessitating repetitive adjustments of DBS parameters, which was likely to be associated with altered neuroplasticity over time.

When DBSWS occurs, battery replacement should be performed urgently, because patients may not respond to immediate conservative treatment. Because increasing numbers of patients with PD are receiving DBS and earlier operations, thus achieving longer disease durations with DBS, DBSWS might become a more common and highly relevant complication of which treating physicians should be aware.

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Disclosures

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